

REMARKS/ARGUMENTS

Amendments to the Claims

Claim 5 has been amended to recite “a plant virus vector comprising a cauliflower mosaic virus promoter.” The specification supports this by disclosing “...driven by a *Cauliflower mosaic virus* (CaMV) 35S promoter to generate *in vivo* infectious transcript.” Specification at page 15 at lines 4-5. Thus, the specification supports the limitation of claim 5.

Claims 14 and 28 have been amended to recite “wherein the dust mite allergen is obtained from the transgenic plant itself....” The specification supports this amendment by disclosing:

There are several strategies for **obtaining the dust mite allergen from** plant cells or whole plants. In one embodiment, the method of obtaining the allergen according to the invention is accomplished by obtaining the plant cell or whole plant or portions thereof such as fruits, leaves, stems, and tubers or extract thereof. In another embodiment, the dust mite allergen is provided by further purifying the allergen from the extract. In still another embodiment, the dust mite allergen is obtained by merely harvesting at least a part of a transgenic plant, such as fruit or seeds. In still another embodiment, the dust mite allergen is provided in the form of the transgenic plant itself.

Specification at page 13, lines 12-21 (emphasis added). Thus, the specification supports the amended claims 14 and 24.

New claim 35 recites “a plant virus vector comprising multiple cloning sites.” The specification supports this on page 15 at lines 7-8 by disclosing “multiple cloning sites (*Nco* I, *Sph* I, *Apa* I, *Mlu* I, *Kpn* I, and *Sac* II)....”

New claim 36 recites “a plant virus vector comprising a GFP coding region.” The specification supports this on page 15 at line 6 by disclosing “...to insert the ORF of GFP (Clontech) between the P1 and HC-Pro coding regions of ZYMV.”

New claim 37 recites “a plant virus vector comprising a NIa-protease cleavage site.” The specification supports this in Figure 1 and on page 5 at line 23 by disclosing “Protease cleavage sites processed by the NIa protease of ZYMV are shown by ‘/’.”

New claims 38 and 39 recite “wherein the vector is a Tobacco mosaic virus (TMV).” The specification supports this on page 9 at lines 23- 24 by disclosing “...zucchini yellow mosaic virus (ZYMV) and tobacco mosaic virus (TMV) are suitable according to the invention.”

No new matter has been added.

Claim Objections

Claim 15 is objected to because of improper claim language. Applicant has amended claim 15 to replace “an dust mite allergen” with “a dust mite allergen.”

Amendments to the Specification

The specification is objected to because the abstract of the disclosure contains “legalese.” Office Action at page 2, lines 10-11. Applicant has amended the abstract to remove the term “The present invention.”

The Rejection of Claims Under 35 U.S.C. §112, Second Paragraph

Claims 5, 6, 9, and 23 stand rejected under 35 U.S.C. §112, second paragraph, as being indefinite.

The Examiner asserts that claims 5 and 6 are indefinite because “the metes and bounds of modified cannot be determined since applicant has not defined said modified.” Office Action at page 3, lines 9-10. Applicant has amended independent claim 5 to remove the word “modified,” addressing the indefinite rejection.

The Examiner also contends that in claims 10 and 24, the phrase “the plant” lacks antecedent basis. Office Action at page 3, line 12. Applicant has amended claims 10 and 24 to address the antecedent basis issue.

Further, the Examiner asserts that in claims 14 and 28, the term “provided” lacks antecedent basis. Office Action at page 3, line 13. Applicant has amended claims 14 and 28, replacing “provided” with “obtained from,” to expedite prosecution.

Claims 5, 6, 9, and 23 as amended fully comply with the requirements of 35 U.S.C. §112, second paragraph, for particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

The Rejection of Claims Under 35 U.S.C. §112, First Paragraph

Claims 5-6 and 19 stand rejected under 35 U.S.C. §112, first paragraph, for not being enabled.

The Office Action asserts that the specification does not “reasonably provide enablement for a modified plant virus vector.” Office Action at page 3, lines 24-25. Independent claim 5 has been amended to remove the term “modified.” To expedite prosecution claim 19 has been canceled. Claims 5 and 6 as amended fully comply with the enablement requirements.

The Rejection of Claims Under 35 U.S.C. §103(a)

Rejection of Claims 1-4, 7-18, and 21-28 under 35 U.S.C. §103(a)

Claims 1-4, 7-18, and 21-28 are rejected as unpatentable over Mason et al. (US 2003/0079248 A1) in view of Hsu et al. (International Immunology, 8:1405-1411, 1996). The rejection is respectfully traversed.

Independent claim 1 recites a process for producing a dust mite allergen comprising the steps of: constructing a vector for plant transformation that comprises a DNA sequence encoding the dust mite allergen operably linked to a plant-specific promoter; transforming a plant cell or tissue with this vector; and obtaining the dust mite allergen from the plant cell or tissue. Independent claim 15 recites a process for producing an antigenic composition, the antigenic composition comprising a dust mite allergen, wherein the dust mite allergen is prepared by a process comprising the steps of constructing a vector for plant transformation that comprises a DNA sequence encoding

the dust mite allergen operably linked to a plant-specific promoter; transforming a plant cell or tissue with this vector; and obtaining the dust mite allergen from the plant cell or tissue.

To reject a claim as *prima facie* obvious three criteria must be met:

First, there must be some suggestion or motivation, either in the references themselves or in the knowledge generally available to one of ordinary skill in the art, to modify the reference or to combine reference teachings. Second, there must be a reasonable expectation of success. Finally, the prior art reference (or references when combined) must teach or suggest all the claim limitations.

MPEP § 2143. The rejection fails to meet the second criterion.

Mason is cited as teaching “a process for producing a protein comprising the steps of: (a) constructing a plant transformation vector that comprises a DNA sequence operably linked to a plant-specific promoter, transforming a plant cell with the vector, and obtaining the protein from the plant cell.” Office Action at page 4, lines 15-18. Hsu is cited as teaching a “dust mite allergen, Der p 5 cDNA, expression of Der p 5, and Der 5 p protein.” Office Action at page 5, lines 1-3.

The Office Action asserts:

It would have been *prima facie* obvious to one of ordinary skill in the art at the time the invention was made to substitute the Der p 5 cDNA taught by Hsu for the BeYDV (for example) protein taught by Mason for the purposes of expressing Der p5 in potato or other edible plant or plant portion to create an edible therapeutic agent. One skilled in the art would have been motivated to generate the claimed invention with a reasonable expectation of success.

Office Action at page 5, lines 5-10.

Applicants respectfully traverse. Contrary to the bald assertion of the rejection, one skilled in the art would not have had a reasonable expectation of success.

At the time of the invention, it was well known in the art that not all foreign proteins are efficiently produced in plants. Vitale and Pedrazzini (Mol Interv. Vol. 5, 216-25, Aug 2005) teaches that plants have a vacuolar sorting pathway that targets some foreign protein to the vacuole leading to protein degradation. “Leaf vacuoles are mainly of the lytic type and can degrade foreign protein, resulting in a loss of product.” Exhibit 1, Page 221, lines 46-48, right hand column. One must empirically determine whether a protein is subject to vacuolar delivery in a plant system. Vitale and Pedrazzini teach that “the possible loss of foreign protein introduced into the plant secretory pathway due to vacuolar delivery must be verified experimentally for each individual protein, and it is very difficult to make predictions.” Exhibit 1, Page 222 at lines 16-19. The vacuolar sorting signals in plants are short amino-acid sequences that are non-canonical and very diverse. Exhibit 1, Page 222 at lines 8-11.

The state of the art as demonstrated by Vitale and Pedrazzini, would have prevented one skilled in the art from having a reasonable expectation of success. One of ordinary skill in the art would not have known if a dust mite allergen would be successfully produced in a plant system until it was determined empirically. Thus, the combination of the Der p 5 protein, expressed in mice, as taught by Hsu et al., with a viral delivery system for plants, as taught by Mason et al. does not present a *prima facie* case. Thus the *prima facie* case fails because one of the three criteria for a *prima facie* case has not been met by the rejection.

Withdrawal of this rejection to independent claims 1 and 15 is respectfully requested. Claims 2-4, 7-14, 16-18, and 21-28 are dependent on claim 1 or 15 and are thus allowable for at least the same reasons as claims 1 and 15 and further in view of the novel and non-obvious features recited therein.

Rejection of Claims 1-3, 5-18, 19-28 under 35 U.S.C. §103(a)

Claims 1-3, 5-18, 19-28 are rejected as unpatentable over Lin et al. (Bot. Bull. Acad. Sin. 43: 261-268, 2002) in view of Hsu et al. (International Immunology, 8:1405-1411, 1996). The rejection is respectfully traversed because the rejection fails to provide a reasonable expectation of success.

The Examiner states that “Lin teaches a ZYMV based system for expressing foreign proteins in cucurbits. ZYMV as (sic) a vector to express foreign proteins of interest.” Office Action at page 5, lines 13-15. The Examiner also states that Hsu teaches “dust mite allergen, Der p 5 cDNA, expression of Der p 5, and Der 5 p protein.” Office Action at page 5, lines 16-17.

The Office Action states:

It would have been *prima facie* obvious to one of ordinary skill in the art at the time the invention was made to substitute the Der p 5 protein of Hsu for the generic foreign protein in the ZYMV vector expression system of Lin for the purpose of expressing Der p 5 in cucurbits such as *Cucurbita pepo* L. var. Zucchini to create an edible therapeutic agent. One skilled in the art would have been motivated to generate the claimed invention with a reasonable expectation of success.

Office Action at page 5, line 19 – page 6, line 3.

As discussed above, successful production of a foreign protein in plants was not predictable as of the effective filing date. It was well known in the art of transgenic plant protein expression that each individual protein requires empirical determination. If a recombinant protein contains a cryptic vacuolar sorting signal, it can be fatally targeted to a plant vacuole where it is degraded. See Exhibit 1.

At most, Lin teaches the construction of a ZYMV vector and verifies the infectivity of the viral vector. Lin at page 266, lines 23-29, left hand column. Lin merely suggests that the insertion capacity of the vector “is suitable for the development of a viral vector for expressing foreign proteins in cucurbits.” Lin at page 267, lines 22-23. Hsu teaches expression of the Der p 5 protein in mice. Hsu et al., Abstract and page 1408, lines 1-3, left hand column. Expression of a dust mite allergen in a mammal is not predictive of successful expression in a plant. As detailed above, expression a foreign protein in a transgenic plant requires empirical determination. Thus, one of ordinary skill in the art would not have had a reasonable expectation of success in combining the Der p 5 protein, expressed in mice, as taught by Hsu et al., with a system for expressing foreign proteins in cucurbits, as taught by Lin et al.

Withdrawal of this rejection to independent claims 1 and 15 is respectfully requested. Claims 2-3, 5-14, and 19-28 are dependent on claim 1 or 15 and are thus allowable for at least the same reasons as claims 1 and 15 and further in view of the novel and non-obvious features recited therein.

Respectfully submitted,

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